# Ets transcription factor Pointed promotes the generation of intermediate neural progenitors in Drosophila larval brains.

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**Public Summary:**
Neural stem cells often produce neurons and glia, two major types of cells that construct the nervous system, indirectly by generating intermediate proliferative precursor cells called intermediate neural progenitor (INPs) cells. INPs undergo several round of divisions to amplify themselves before they divide terminally to produce neurons and glia. The transient proliferative divisions of INPs significantly amplify the number of neurons and glia derived from neural stem cells and increase the brain surface area. In the larval brains of fruit flies, INPs are produced from one particular type of NSCs, which is called type II neuroblasts (NBs). Type II NBs differ from type I NBs by their lack of the expression of a protein called Asense (Ase), which regulates the expression of genes important for the development of nervous system. However, why Ase expression is suppressed in type II NBs and why only type II NBs produce INPs are not understood. Our studies show that one particular form of a gene regulatory protein called Pointed (Pnt), PntP1, is specifically expressed in type II NBs as well as newly generated INPs. Partial loss of PntP1's function or inhibiting PntP1activity by expressing another protein Yan, which prevent Pnt from activating gene expression, results in a reduction or elimination of INPs and abnormal expression of Ase in type II NBs. Conversely, forced expression of PntP1 in type I NBs suppresses Ase expression in the NBs and induced the generation of INP-like cells from type I NBs. Like in normal type II NBs, the PntP1-induced generation of INP-like cells in type I NBs also depends on the activity of a protein called Brain tumor, which normally suppresses brain tumor formation. Our findings suggest that PntP1 is both necessary and sufficient for the suppression of Ase in type II NBs and the generation of INPs in the larval brain of fruit flies.

**Scientific Abstract:**
Intermediate neural progenitor (INP) cells are transient amplifying neurogenic precursor cells generated from neural stem cells. Amplification of INPs significantly increases the number of neurons and glia produced from neural stem cells. In Drosophila larval brains, INPs are produced from type II neuroblasts (NBs, Drosophila neural stem cells), which lack the proneural protein Asense (Ase) but not from Ase-expressing type I NBs. To date, little is known about how Ase is suppressed in type II NBs and how the generation of INPs is controlled. Here we show that one isoform of the Ets transcription factor Pointed (Pnt), PntP1, is specifically expressed in type II NBs, immature INPs, and newly mature INPs in type II NB lineages. Partial loss of PntP1 in genetic mosaic clones or ectopic expression of the Pnt antagonist Yan, an Ets family transcriptional repressor, results in a reduction or elimination of INPs and ectopic expression of Ase in type II NBs. Conversely, ectopic expression of PntP1 in type I NBs suppresses Ase expression the NB and induces ectopic INP-like cells in a process that depends on the activity of the tumor suppressor Brain tumor. Our findings suggest that PntP1 is both necessary and sufficient for the suppression of Ase in type II NBs and the generation of INPs in Drosophila larval brains.

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